REMARKS

Reconsideration of the present application in view of the above amendments and following remarks is respectfully requested. Claims 1, 2, 4, 12, 13, 15-18, 20, 29, 31, 32, 35-37, 40-42, 44, 45, and 47-64 were pending. As set forth above, Applicants have hereby amended claims 1, 20, 29, 41, and 42 to more clearly define the subject matter encompassed by the Applicants' invention, and hereby amended claims 50, 63, and 64 for mere editorial purposes to remove an obvious inadvertent typographical error (*i.e.*, to remove redundant reference to indolicidin analogs). Support for the amendment of claims 1 and 29 may be found in the specification as originally filed, for example, at page 26, lines 8-12. In particular, the exemplary indolicidin analogs, MBI 11 and MBI 11B7, retain at least 30% tryptophan of wild-type indolicidin. Applicants hereby submit new claims 65-67. Support for the new claims may be found in the application as originally filed (*see, e.g.*, page 8, line 29 through page 9, line 4; page 6, lines 16-20; page 21, line 29 through page 22, line 16; page 33, line 30; Example 11; and Table 3 of Example 14). No new matter has been added. Therefore, claims 1, 2, 4, 12, 13, 15-18, 20, 29, 31, 32, 35-37, 40-42, 44, 45, and 47-67 are currently pending.

INFORMATION DISCLOSURE STATEMENT

As previously made of record, Applicants submit that reference AD (U.S. Patent No. 6,242,219 to Better) of the Second Supplemental Information Disclosure Statement filed on November 27, 2001 was inadvertently not initialed as considered by the Examiner. Applicants respectfully request that this reference be confirmed as considered. Applicants enclose a copy of Form 1449, page 1 of 1, and reference AD for the Examiner's convenience.

REJECTION UNDER U.S.C. §102(e)

In the Office Action, claims 1, 2, 4, 16, 17, 18, and 20 have been rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 5,851,802 (Better). In particular, it is asserted that Better teaches a fusion protein expression cassette comprising a nucleic acid molecule that encodes a polypeptide having the structure (cationic peptide)-[(cleavage site)-(cationic peptide)]$_n$ wherein n has a value up to 4, as claimed. Furthermore, it is asserted that the

claims are unclear as to what is considered an "indolicidin analog" and, thus, the peptides of the antimicrobial bactericidal/permeability increasing (BPI) protein disclosed by Better are considered "analogs" of indolicidin.

Applicants respectfully traverse this ground of rejection and submit that Better fails to teach or suggest every limitation of the instant claims and, therefore, fails to anticipate the claimed invention. As described in the specification and recited in the currently pending claims, the instant invention is directed, in pertinent part for this rejection, to a fusion protein expression cassette, comprising a promoter operably linked to a nucleic acid molecule that encodes an indolicidin analog fusion protein, wherein the encoded fusion protein comprises a structure of (indolicidin analog)-[(cleavage site)-(indolicidin analog)]$_n$ with n being an integer having a value between one and three, and wherein the indolicidin analogs retain at least 30% tryptophan and have antimicrobial activity. As previously made of record, Better merely describes nucleic acid expression constructs for BPI peptides only and is silent with regard to any other cationic peptide. Moreover, a person having ordinary skill in the art would clearly understand that indolicidin analogs versus peptides derived from BPI are different molecules. Nevertheless, however, as discussed in more detail below and merely to expedite allowance of the instant application, claim 1 has been amended to further define an "indolicidin analog" as retaining at least 30% tryptophan and having antimicrobial activity. All of the peptides provided by Better, therefore, fail to teach or suggest an indolicidin analog according to the instant invention, much less a fusion protein expression cassette as claimed.

Accordingly, Applicants respectfully submit that the instant claims are patentably distinct over Better and, therefore, satisfy the requirements of 35 U.S.C. §102(e). Applicants request that this rejection be withdrawn.

REJECTION UNDER U.S.C. §103(a)

In the Office Action, claim 15 was rejected under 35 U.S.C. §103(a) as unpatentable over Better (U.S. Patent 5,851,802) in view of Shen *et al.* (*Proc. Natl. Acad. Sci. 81(15)*: 4627, 1984), the Stratagene Catalog (pp. 38, 44 and 48, 1993), the Pharmacia Product Catalog (pp. 110, and 121-123, 1996), and Sambrook *et al.* (*Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, pp. 1.14 – 1.15, 1989). In particular, it is asserted

that it would have been obvious for a person having ordinary skill in the art to replace the promoter taught by Better for one of the promoters taught by Sambrook *et al.*, as motivated by the materials available in the laboratory.

Applicants respectfully traverse this ground of rejection and submit that the cited references, taken alone or in combination, fail to teach or suggest the claimed invention. As set forth above, Better fails to teach or suggest a fusion protein expression cassette according to the instant claimed invention. Furthermore, Applicants submit that Shen *et al.*, the Stratagene Catalog, the Pharmacia Product Catalog, and Sambrook *et al.*, alone or in combination, do not cure the deficiencies of Better. Each of the cited references merely provide additional promoters that can be used in an expression, which is merely cumulative subject matter taught in the instant specification. For example, the instant specification discloses several promoters useful in expression constructs that are well-known in the art (*see, e.g.*, specification at page 23, lines 4-12 and references cited therein). Furthermore, because each of Shen *et al.*, the Stratagene Catalog, the Pharmacia Product Catalog, and Sambrook *et al.* is a general reference regarding, *inter alia*, promoters for expression vectors, each cited reference fails to teach or suggest the fusion protein expression cassette of the instant invention, much less indolicidin or indolicidin analogs. In addition, Applicants respectfully submit that the mere fact that the teachings of the prior art *can* be combined or modified, or that a person having ordinary skill in the art is *capable* of combining or modifying the teachings of the prior art, does not make the resultant combination *prima facie* obvious, as the prior art must also suggest the desirability of the combination (*see, e.g., In re Mills*, 16 USPQ2d 1430, Fed. Cir. 1990; *In re Fritch*, 23 USPQ2d 1780, Fed. Cir. 1992).

Applicant, therefore, respectfully submits that the Patent Office has not set forth a *prima facie* case of obviousness because the cited references, taken alone or in combination, fail to teach every limitation of the instant invention and fail to provide motivation for a person having ordinary skill in the art to modify or combine the prior art teachings to arrive at the claimed invention with a reasonable expectation of success. Accordingly, applicants respectfully request that this ground of rejection be withdrawn.

REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

In the Office Action, claims 1, 2, 4, 12, 13, 15-18, 20, 29, 31, 32, 35-37, 40-42, 44, 45, and 47-64 were rejected under 35 U.S.C. §112, second paragraph, as indefinite. In particular, it is asserted that (1) the metes and bounds of the phrase "indolicidin analogs" recited in claims 1 and 29 is not clear because the specification allegedly provides only one indolicidin sequence and allegedly does not provide any definition as to what sequences are considered "indolicidin analogs;" (2) that the recitation of "at least one indolicidin analog" in claims 20 and 50 is indefinite because the claims from which they ultimately depend (claims 1 and 29, respectively) specify an expression cassette that would produce a fusion protein having at least two indolicidin analogs; and (3) that claims 41 and 42 are unclear because the specification does not define how many indolicidin analogs are encompassed by the term "about," and that claim 41 is unclear as to the position of the indolicidin analogs relative to the fusion protein. Each of these rejections will be addressed in turn below.

(1) Applicants respectfully traverse this ground of rejection and submit that what is meant by "indolicidin analog" is clear to a person having ordinary skill in the art, as recited in the claims and described in the specification. The term "analog" has a plain and ordinary meaning and is a term commonly used in the art (*see, e.g.*, specification at page 10, lines 27-28; at page 13, lines 22-29; at page 19, line 10 through page 20, line 26; at page 26, lines 8-14; claims of U.S. Patent No. 6,180,604, Fraser *et al.*, provided herewith in the third Supplemental Information Disclosure Statement). In addition, a person having ordinary skill in the art would understand that an "indolicidin analog" would be, for example, a structural variant derived from naturally occurring indolicidin (*see, e.g.*, page 26, lines 8-14 and references cited therein). Nevertheless, however, merely to expedite allowance of the instant application, claims 1 and 29 have been amended to more clearly define an "indolicidin analog" as retaining at least 30% tryptophan and having antimicrobial activity. Applicants respectfully submit that two illustrative indolicidin analogs are described (*see, e.g.*, specification at page 26, lines 11-12), which are exemplary of other analogs described in, for example, WO 97/08199 and WO 98/07745 (*see, e.g.*, specification at page 26, line 13). For example, wild-type indolicidin (I L P W K W P W W P W R R, the amino acid sequence of which was known in the art at the time of filing the instant application) contains approximately 38% tryptophan, while indolicidin analog

MBI 11 retains approximately 30% tryptophan and MBI 11B7 retains approximately 33% tryptophan of the tryptophan in wild-type indolicidin. Therefore, Applicants submit that currently pending claims 1 and 29 are sufficiently clear for a person having ordinary skill in the art.

(2) With regard to the alleged indefiniteness of the recitation "at least one indolicidin analog," Applicants respectfully traverse. Applicants respectfully submit that claim 50 ultimately depends from claim 29, which, contrary to the assertion in the Office Action, is not so limited as to require two indolicidin analogs within the fusion protein. Nonetheless, Applicants believe that the recitation of "at least one indolicidin analog" is redundant in claims 50, 63, and 64. Therefore, Applicants have deleted the phrase "at least one indolicidin analog" from claims 20, 50, 63, and 64. Hence, Applicants submit that this ground of rejection has been rendered moot.

(2) With regard to the alleged indefiniteness of the recitation "about" and the clarity of the position of the indolicidin analogs relative to the fusion protein, Applicants respectfully traverse. In particular, Applicants submit that this ground of rejection has been rendered moot because the phrase "about" has been deleted from claims 41 and 42. Furthermore, Applicants wish to thank the Examiner for suggesting clarifying language for claims 41 and 42, which Applicants have included in these claims. Therefore, this ground of rejection has also been rendered moot.

Accordingly, Applicants respectfully submit that the invention as presently claimed satisfies the definiteness requirements of 35 U.S.C. §112, second paragraph and, therefore, request that these rejections be withdrawn.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims pending in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. The Examiner is urged to contact the undersigned attorney if there are any questions prior to allowance of this matter.

Respectfully submitted,

Jan Burian and Daniel Bartfeld

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PATENT TRADEMARK OFFICE

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Enclosures:

Copy of Form 1449, page 1 of 1
Reference AD
Third Supplemental IDS
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8 references

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